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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/596,507	06/19/2000	Horst Peschel	4070-174US (K400417US)	3984
570	7590	07/13/2004	EXAMINER	
AKIN GUMP STRAUSS HAUER & FELD L.L.P. ONE COMMERCE SQUARE 2005 MARKET STREET, SUITE 2200 PHILADELPHIA, PA 19103-7013			HAYES, ROBERT CLINTON	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/596,507	PESCHEL, HORST	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-49,51-53,63,70-79,83 and 84 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-49,51-53,63,70-79,83 and 84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/28/04 has been entered.
2. The rejection of claims 44-49, 51-54, 58-61, 63-64, 66-78 under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "differentiating-promoting factors" is withdrawn due to the amendment or cancellation of the claims.
3. Applicant's arguments filed 4/28/04 have been fully considered but they are not persuasive.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Claim 52 stands objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form, for the reasons made of record in Paper NOs: 9 (mailed 4/9/02), 12 (mailed 11/05/02) & 16 (mailed 7/21/03) and as follows.

In contrast to Applicant's assertions on page 6 of the response, base claim 44 is directed to "a neuronal **tissue** *derived from a brain or spinal cord*" [emphasis added], in which brain or spinal cord *tissue* intrinsically comprises many different types of cells, and therefore, remains not reasonably "derived from a single cell" **after-the-fact** as still claimed in dependent claim 52.

6. Claims 44-49, 51-53, 63, 70-79 & 83-84 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record for cancelled claims 26-43 in Paper NOs: 9 (mailed 4/9/02), 12 (mailed 11/05/02), & 16 (mailed 7/21/03), and as follows.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant specification continues to exist for the following claim recitations, in contrast to Applicant's assertions on pages 6-9 of the response. For example, base claims 44 & 63 now recite "a differentiation-promoting factor selected from the group consisting of...", which alternatively is generically described on pages 5-6 of the specification to "promote differentiation in specific neurons", which include all neurons. In contrast, the claims are directed to only a capability of differentiating to *dopaminergic neurons*, for which the specification discloses on pages 6 & 11 that only GDNF, LIF, IL1 (IL-1b), IL-11

and thyroid hormone can be used to accomplish such, versus the broader scope of using the currently recited additional factors, which alternatively are described in context within the specification for differentiating neuronal progenitor cells into different neuronal populations; thereby, constituting new matter. Second, in contrast to Applicant's assertions on page 9 of the response, page 2 of the specification alternatively contemplates "[t]he percentage of such *specific* [differentiated] **neurons** in the tissue samples should be greater than 90%, preferably greater than 95%[emphasis added]", which remains entirely different in antecedent basis and conception to that currently recited in which "neuron **progenitors**" are "more than 90/95% of cells in the neuronal tissue", as it relates to claims 45 & 46, and as similarly recited in claim 70, as previously made of record. Third, in contrast to Applicant's assertions on page 9 of the response, no where on page 5 of the specification does proper basis exist for the recitation of "*partial differentiation* is performed **more than once**" (i.e., as it relates to claim 71) and/or "proliferating the *subcloned* partially differentiated...", versus the different concepts of "**dedifferentiation**" and "priming", as alternatively described on page 5, lines 2-16. Forth, no proper antecedent basis nor conception exists within the specification for the recitation of "step c) is conducted at *sub-atmospheric oxygen level*", or "at least one of the proliferation, partial differentiation, and subcloning steps is conducted at *sub-atmospheric oxygen levels*" (i.e., as it relates to claims 72-74); thereby, constituting new matter. Fifth, claims 75 & 76 still recite for "wherein at least one of the steps of proliferation, partial differentiation, and subcloning steps is conducted at a condition which simulates reduced atmospheric oxygen content", versus that disclosed on page 4 wherein oxygen content is reduce for only the "expansion state"; thereby, still constituting new matter. Sixth, the recitation of "wherein the single progenitor cell is selected on the basis that it

expresses a marker characteristic of the selected type of neuron” (i.e., as it relates to claim 83) still constitutes new matter because these progenitor cells are not transfected, which is different in scope from that described within the specification, and would further constitute a different nonelected invention. Lastly, the additional method steps recited in claim 63(f) or claim 79b still constitutes new matter, which Applicant has chosen to also not addressed.

It is strongly suggested that Applicant no longer attempts to broaden that described within the specification at the time of filing the instant application by continuing to mix and match different concepts from the specification, and alternatively claim that invented at the time of filing the instant specification. In other words, although Applicant is correct that what is claimed does not require an “*in hac verba*” recitation from the specification, the subtle nature of the terminology used within the art warrants more accurate and less ambiguous and/or broad recitations from that originally submitted at the specification at the time of filing this application.

7. Claims 79 & 83-84 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper NOs: 9 (mailed 4/9/02) & 12 (mailed 11/05/03), & 16 (mailed 7/21/03), and as follows.

As previously made of record, the specification still fails to define the metes and bounds that the term “differentiating-promoting factors” encompasses, in which no universal differentiating-promoting factor exists nor would all cells encompassed by the claims reasonably

express receptors to all such putative factors (if known). In contrast to Applicant's assertions, Applicant did not amend these claims.

8. Claims 44-49, 51-53, 63, 70-79 & 83-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what exactly the recitation of "partially differentiated" entails as used in the instant claims, due to Applicant's comments on page 13 of the response that this term defines a "new terminology". In contrast, neuronal progenitor cells are already partially differentiated from multipotent neural stem cells, and therefore, are already committed to differentiating into neurons (i.e., "partially differentiated"), yet probably not yet committed to the terminally differentiated state of a specific neuronal population (e.g., dopaminergic neurons). Alternatively, neuronal progenitor cells may be "primed" to a specific neuronal population fate depending on the presence of specific differentiating factors. Alternatively, "partially differentiated" could represent a population of neuronal progenitor cells in which some have terminally differentiated, whereas others have yet to differentiate into a specific population of neurons (e.g., as it relates especially to claims 45-46 & 70). In other words, Applicant is not permitted to change the meaning of a term. No term may be given meaning repugnant to the usual meaning of the term (see MPEP 608.01 (o)), as already made of record.

9. Claims 79 & 83-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of “the neuronal tissue [is] made by transiently contacting in vitro... ii) a differentiation-promoting factor” makes little sense, because why would contacting a “differentiation-promoting factor” make neuronal tissue, as currently recited in claims 79 & 83.

Second, claim 83 recites “wherein substantially all are of the neuronal progenitor cells in the neuronal tissue...”, which makes little grammatical sense. In addition, the recitation of “substantially” is a relative term that is indefinite, because it is unclear when something is alternatively no longer “substantially all”; especially if such cells are also to be “partially differentiated”. Note that the recitation of “capacity to perform mitosis” does not require mitotically dividing cells, only that they are capable of undergoing mitosis (e.g., after dedifferentiation, etc.). For example, claim 83 recites “expresses a [terminally differentiated] marker characteristic of the dopaminergic neuron”, yet claims 79 & 84 require “capability of the progenitor cell to perform mitosis” or proliferate, which is contradictory.

Third, no antecedent basis no longer exists in claim 79 for the recitation of “synthetic tissue” in line 7.

10. Claims 44-49, 51-53, 63, 70-79 & 83-84 stand rejected under 35 U.S.C. 102(b) as being anticipated by Boss et al. (US Patent 5,411,883; IDS Ref #3), for the reasons made of record in Paper NOs: 9 (mailed 4/9/02), 12 (mailed 11/05/03) & 16 (mailed 7/21/03), and as follows.

In contrast to Applicant's assertions on pages 10-13 of the response, Boss clearly teach partially differentiated neural progenitor cells as illustrated by Boss' claim 1, in which Boss' neuronal progenitor cells further “***are capable of*** differentiating into *substantially* only dopaminergic neurons”, as illustrated in columns 17-18 & 19-20, and as previously made of record. Thus, Applicant's arguments are clearly not on point with that claimed, because it is immaterial whether, or not, Boss' terminally differentiated dopaminergic neurons are “no longer mitotic”, because the claims are directed to “partially differentiated neuronal progenitor cells”, which Boss et al clearly teach.

The Schwarz Declaration filed 4/28/04 is not persuasive because it appears to rely on “German law” (e.g., see page 5 of the declaration), and because it mischaracterizes the teachings of Boss et al. (and Luskin et al) by either apparently trying to confuse the record by arguing about what “neural progenitor/stem cells” constitute (which is a different teaching and concept not claimed), or by concentrating only on Boss' illustration of their cells being “capable of differentiating into substantially only dopaminergic neurons” “that are no longer mitotic”, none of which reasonably constitutes “evidence to show that neither Boss nor Luskin teaches a neuronal tissue that is made of partially differentiated *neural (sic)* progenitor cells... “, as asserted by declarant. In other words, Declarant's opinion summarized on page 7 of the declaration, as it relates to “no technical or scientific basis” for the instant rejections, ignores the current claim language, ignores the rejection made of record in light of the current claim language, and appears to question the validity of a U.S. patent claiming mammalian/human “neuronal progenitor cells”. *In arguendo*, it is inconsistent to assume that Boss' cells are not neuronal progenitor cells that “do not undergo mitosis” when they “propagate” in culture, which

is impossible unless they are capable of undergoing mitosis, by definition. Second, because Boss was able to demonstrate that their cells terminally differentiate into “substantially dopaminergic neurons upon contact of the ... tissue with a differentiation-promoting factor”, Boss et al reasonably teach the instant invention, as illustrated by Boss' claim 1; consistent with that held by the U.S. courts in *Ex parte Gray*, *In re Best*, *In re Thorpe* and *In re Marosi*, previously made of record. Again, as previously made of record,

“the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved”. *Ex parte Gray*, 10 USPQ 2d 1922 (1989); *In re Best*, 195 USPQ 430 (CCPA 1976).

Thus, Applicant's and Declarant's arguments are not persuasive.

11. Claims 44-49, 51-53, 63, 70-79 & 83-84 stand rejected under 35 U.S.C. 102(b) as being anticipated by Emory University/Luskin et al. (WO 97/02049; IDS Ref #10), for the reasons made of record in Paper NOs: 9 (mailed 4/9/02), 12 (mailed 11/05/03) & 16 (mailed 7/21/03), and as follows.

In contrast to Applicant's mischaracterization of what Luskin teach on page 12 of the response, and the comments on page 5 of the Schwarz Declaration, Luskin et al teach isolation of human and mammalian brain-derived neuronal progenitor cells capable of differentiating into >90% dopaminergic neurons (e.g., pgs. 7, 9 (lines **14-18**), 11, 14 & 29). Luskin's progenitor cells further contain less than 5%, and even less than 2% glial cells (i.e., including “immuno-competent glial cells”), as described on pages 8, 11 & 21. Therefore, Applicant's and Declarant's

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arguments are not persuasive for the reasons made of record, which is further consistent with that held by the courts in *Ex parte Gray*, *In re Best*, *In re Thorpe* and *In re Marosi*, previously made of record.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax phone number for this Group is (703) 872-9306.



Robert C. Hayes, Ph.D.

July 1, 2003

**ROBERT C. HAYES, PH.D.
PATENT EXAMINER**